7. (once amended) An isolated nucleic acid comprising a polynucleotide having at least about 90% identity with SEQ ID NO: 2 wherein the encoded polypeptide possesses enzymatic activity.

8. (once amended) An isolated nucleic acid according to claim 7 comprising SEQ ID NO: 2.

C15

Remarks

The Office Action mailed May 3, 2002 has been carefully reviewed and the foregoing amendment has been made in consequence thereof.

Claims 1-37 are now pending in this application. Claims 1-5 and 7-8 stand rejected. Claims 6 and 9-37 stand withdrawn from consideration by the Examiner as subject to a Restriction Requirement made Final.

In accordance with 37 C.F.R. 1.136(a), a three month extension of time is submitted herewith to extend the due date of the response to the Office Action dated May 3, 2002 for the above-identified patent application from August 3, 2002 through and including November 3, 2002. This response is timely filed on Monday November 4, 2002, the next business day following Sunday November 3, 2002. In accordance with 37 C.F.R. 1.17(a)(3), authorization to charge a deposit account in the amount of $460.00 to cover this extension of time request also is submitted herewith.

The specification has been amended at several pages to conform the SEQ ID numbering to the Sequence Listing. The SEQ ID numbers of Sequences including SEQ ID 1 and 5, has been corrected to correspond to the sequence listing. Claims 3, 6-8 have been amended to confirm language to the elected products of the Restriction Requirement made final and to conform the SEQ ID numbering to the sequence listing. No new matter is presented by this amending. Claim 3 now refers to a polynucleotide sequence. Claims 3, 6-8 are thus free of the Examiner's objection which is requested to be withdrawn. The specification is believed to meet all sequence listing requirements and rules therefor.

The rejection of Claims 1-5 and 7-8 under 35 U.S.C. § 112, first paragraph as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s) at the time the application was filed had possession of the claimed invention is respectfully traversed in its entirety.

Applicants submit that the specification provides numerous sequences which describe the variants of the phospholipase $A_{2\gamma}$. This refutes the Examiner's unsubstantiated and unsupported contention s. Applicant has shown in the specification more than sufficient detail regarding the claimed invention to satisfy 35 U.S.C. Section 112, all paragraphs. This detail appears in the specification for example at pages 5 and 6. Additionally the Examiner asserted that applicants have provided a description of only one member of this genus which is not representative of the variants of the genus. This assertion is respectfully traversed in that applicant has provided instances of representatives (variants) of this genus in particular in the detailed description provided on pages 5 and 6 of the specification. Additionally the Examiner assert that the specification does not disclose the identifying characteristics which would allow one to recognize a nucleic acid molecule as being a phospholipase $A_{2\gamma}$. This assertion is also respectfully traversed. Applicants wish to point out that the identification of a sequence as being a phospholipase $A_{2\gamma}$ (iPL $A_{2\gamma}$) is made by performing NCBI Blast analysis (http://www.ncbilnlm.nih. Gov/BLAST/) of the sequence in question. Identify or a high degree of alignment with (SEQ ID NO: 3) will characterize the sequence as $iPLA_{2\gamma}$ or a homolog thereof. Further as applicant has recited in the specification on page 5 : "The $iPLA_{2\gamma}$ polypeptides within the present invention are also intended to include $iPLA_{2\gamma}$ of any origin which are substantially identical to and which are biologically equivalent to the $iPLA_{2\gamma}$ polypeptides characterized and described herein." Sufficient identifying characteristics are thus provided.

For at least the reasons set forth above, Applicants respectfully request that the Examiner's Section 112 rejections of Claims 1-5 and 7-8 has been overcome and should be withdrawn.

The Examiner noted that original Claim 7 is drawn to a polynucleotide having at least about 90% sequence identify with SEQ ID NO: 3 with no limitations placed on the encoded polypeptide. Additionally the Examiner asserted that the specification does not describe the function of all the polypeptide sequences derived or modified form SEQ ID No:1 and therefore, many functionally unrelated polynucleotides are encompassed within the scope of these claims. Therefore according to the Examiner the instant application fails to describe representative species by identifying characteristics or structural properties other than comprising of SEQ ID NO: 3. All these assertions of the Examiner are respectfully traversed.

As applicants have noted; the specification recites on pages 5: "The $iPLA_{2\gamma}$ polypeptides within the present invention are also intended to include $iPLA_{2\gamma}$ of any origin which are substantially identical to and which are biologically equivalent to the $iPLA_{2\gamma}$ polypeptides characterized and described herein.". This is clearly a description of representative species by identifying characteristics or structural properties other than comprising of SEQ ID No: 3 which applicant contends is sufficient of itself to satisfy 35 USC 112.

Applicants wishes to note that Claim 7 meets the requirements of 35 USC 112 as original filed but now has been amended by addition of the phrase wherein the encoded polypeptide possesses enzymatic activity. Thus Claim 7 meets the requirements of 35 USC 112 in all regards in particular by reciting an associated functionality. Applicants thus properly describe representative species by identifying functionality characteristics and thus the specification sufficiently describes the claimed invention in such full , clear, concise and exact terms that a skilled artisan would recognize that applicants were in possession of the inventions of Claims 1-5 and 7-8. The application and all claims meet the requirements of 35 USC 112 in all regards. This rejection is overcome and should be withdrawn.

Applicants wish to point out that variant polypeptides (SEQ. ID 1 etc) can be prepared using methodology of Mancuso et al J. Bio. Chem 2000 275: 9937-9945) In brief, PCR conditions employed include a 30-cycle reaction with steps at 53 C for 30 s, 72 C for 2 min, and 94 C for 30 s per cycle. IPL $A_{2\gamma}$ was amplified utilizing oligos which flanked the predicted 5'and 3' coding region. Human smooth muscle and human skeletal muscle Quick-

Clone cDNA (Clontech) from a human heart cDNA library can be used as a template for preparing the full length construction (SEQ ID NO:1) while the clone derived form this PCR can be used for preparation of the truncated constructs. PCR products are resolved by 1% agarose gel electrophoresis. The PCR band was extracted from agarose with a QIAquick Gel extraction kit and blunt ligated into pGEM-T Vector (Promega). Following bacterial transformation and growth of bacterial transformants, plasmids were prepared using a Qiafilter Plasmid kit (Clontech) and subjected to automated sequence analysis using an ABI 373 Automated DNA sequencer. The cloned inserts from each of these constructs can then be subcloned into an expression vector such as the baculoviral expression vector pFASTBAC (Invitrogen) for expression of recombinant protein. The expressed proteins can be resolved on SDS PAGE for analysis of their molecular mass, used in a phospholipase A2 assay system for analysis of enzymatic activity, or purified for mass spectral analysis or other analysis to characterize protein modification such as phosphorylation or acylation. Each of the variant forms can be cloned into appropriate vectors and used to generate transgenic mice for analysis of systemic effects of overexpression of the recombinant protein such as effects on lipid composition of membranes, propensity to develop myocardial disorders or diabetes.

The Examiner's rejection of Claims 1-5 and 7-8 under 35 U.S.C. § 112, first paragraph for lack of enablement is traversed. These claims are enabled. The Examiner asserted that the specification does not reasonably provide enable for polypeptides with structures different from SEQ ID NO.1. Further the Examiner asserted that the specification does not reasonably provide enable for variant polypeptides of SEQ ID No:1 having unknown function. The Examiner also asserted that the specification while teaching how to make and use the polynucleotide encoding the phospholipase $A_{2\gamma}$ of SEQ ID NO: 1 do not teach which amino acids of SEQ ID 1 can be modified without affecting the functional properties of the polypeptide. All these assertions of the Examiner are respectfully traversed and should be withdrawn. Applicants wish to point out that the immediately foregoing applicants' paragraph demonstrates how variant polypeptides are particularly enabled and described in the specification. The enablement of the claimed is clearly detailed and present in this specification and the enabling specification in particular pages 5 and 6 for example are directed to the claimed invention.

Additionally applicant wishes the Examiner to note that while Fig 13 shows that the lipase active site is localized to amino acids 481-485, this site is believed to be the focal point for the enzymatic activity of $iPLA_{2\gamma}$, it is expected that modifications such as removal of an N-terminal membrane binding domain through use of a downstream ATG start site or use of an alternative promoter will have effects on the functional properties of the polypeptide. These changes may increase or decrease enzymatic activity or specificity or change the intracellular site at which the polypeptides activity is exerted. In fact, the central thrust of the invention is to cover the diversity of the claimed invention in terms of splicing variants, use of alternative promoters and use of downstream ATG start sites with the implication being that the functional properties of this polypeptide are highly regulated by this diverse modification. (For example, see pages 5 and 6 of the specification.)

Each of the $iPLA_{2\gamma}$ variants contains the original lipase active site of the full length iPL $A_{2\gamma}$ (Seq ID1 and thus may be expected to have phospholipase A2 activity. The fact that when the full length form is expressed in the baculovirus system and in transgenic mice, the 74 and 63kDa forms are expressed, may indicated that the true endogenous activity derives from these truncated forms.

Thus, all of the Examiner's rejections under 35 USC 112 are overcome and are requested to be withdrawn.

The rejection of Claims 1-5 under 35 U.S.C. § 102(a) as being anticipated by Mancuso et al. is respectfully traversed. Under US patent law, applicant's disclosure of his or her own work within the year before the application filing date cannot be used against him or her under 35 U.S.C. 102(a) See In re Katz, 215 USPQ 14 (CCPA 1982)

35 U.S.C. 102 provides conditions for patentability; novelty and loss of right to patent as:

A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for patent,.....

In this instance Richard W. Gross and David J. Mancuso the named inventors of this application are two of the three co-authors of the Examiner cited Mancuso et al technical publication. The third co-author is Christopher M. Jenkins. Therefore, by application of MPEP Section 2132.0, wherein the applicants are two of the three co-authors of a publication cited against his or her application, the Mancuso et al. technical publication is removed as a reference by the filing of disclaiming affidavits made out by the other author (Christopher M. Jenkins). This filing establishes that the relevant portions of the publication originated with, or were obtained from, applicants. Ex parte Hirschler, 110 USPQ 384 (Bd. App. 1952). Each of the respective affidavits filed herewith by RichardW. Gross and David J. Mancuso the inventors of the instant application individually affirm that the cited Mancuso et al. technical article is their own work. Further Applicants requested removal of the Mancuso et al as a reference is in accordance with MPEP Section 2132.01 that such 102(a) rejections can also be overcome by submission of a specific declaration by the applicant establishing that the article is describing applicant's own work (See In re Katz, 215 USPQ 14 (CCPA 1982)). This request to remove Mancuso et al. as a reference here is further supported by the affidavits of Richard W. Gross and David J. Mancuso. Thus this rejection is overcome for at least the aforementioned reasons and should be withdrawn.

The rejections Claims 1-2 and 4-5 under 35 USC 102(b) as being anticipated by Jones et al is respectively traversed.

Applicants claimed invention is patentably distinct over Jones et al in that the claimed invention is encoded by separate genes on a different chromosome, the genes of the claimed invention containing 13 exons whereas Jones et al contains 16 exons, applicants sequence ID 1 gene for example, has two promoters (alternatively spliced exons 1 and 2) and has different intracellular localizations for SEQ ID NO:1 as compared to Jones et al. Applicants claimed invention is peroxisome versus mitochondria for Jones et al. and Applicant's membrane is associated. The claimed polypeptide having SEQ ID NO:1 has potential 88, 77, 74, and 63kD. Thus applicant's claimed invention is patentable over Jones et al. The Examiner's rejection over Jones et al. is overcome and should be withdrawn.

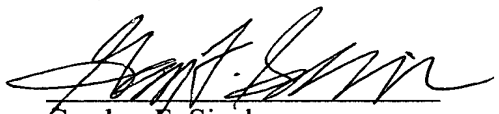
Claims 1-5 depend, directly or indirectly, from independent Claim 1. When the recitations of Claims 2-5 are considered in combination with the recitations of Claim 1, Applicants submit that dependent Claims 2-5 likewise are patentable over the cited references. For the reasons set forth above, Claims 1-5 and 7-8 are submitted to be patentable over the cited references.

Claim 8 depends, directly or indirectly, from independent Claim 7. When the recitation of Claim 8 is considered in combination with the recitation of Claim 7, Applicants submit that dependent Claim 8 likewise is patentable over the cited references.

All the objections have been met and overcome. All the rejections have been traversed and overcome. All objections and rejections are requested to be withdrawn.

In view of the foregoing amendments and remarks, all the claims now active in this application are believed to be in condition for allowance. Reconsideration and favorable action is respectfully solicited. Early passage to issue is requested.

Respectfully Submitted,



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Attached and made a part thereof:

1) Declaration of Richard W. Gross
2) Declaration of David J. Mancuso
3) Declaration of Christopher M. Jenkins